

REMARKS

Claims 73-80 are pending in the application. Applicant has amended claims 73 and 77, which are fully supported by the specification, as set forth below.

35 USC § 112

The Examiner rejected claims 73-80 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In claim 73, the word “association” has been deleted. This amendment finds direct support in the specification. On page 9, lines 20-21, the specification states, “Formononetin or daidzein are preferably administered to a subject substantially unaccompanied by other isoflavones. By this is meant that any composition or preparations may contain minor amounts of other isoflavones, in the order of 10% (w/w) or less.”

In addition, “biochanin” has been amended in claim 73 to specify “biochanin A.” On page 3, lines 28-30, the specification states, “One of the fermentation processes is to demethylate isoflavones (e.g. formononetin gives daidzein and biochanin gives genistein on demethylation).” The Merck Index lists Biochanin A as the 4'-Methyl ether of genistein. (See attached copy of page 744 of the Merck Index listing for genistein.) Hence, the specification would inform a practitioner skilled in the art that the invention includes biochanin A when it refers to the demethylation of biochanin.

The Manual of Patent Examining Procedure (MPEP) provides the following guidance: “What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.... If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.” MPEP § 2163,

citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) and *Martin v. Johnson*, 454 F.2d 746, 751 (CCPA 1972).

In claim 77, the word “derived” has been replaced by “purified” and the plant extracts have been specified to come from the genus *Leguminosae*. Support for these amendments can be found in the specification at page 10, lines 21-26. “Formononetin and daidzein may be prepared ... by purification from extracts of plants of the genus *Leguminosae*....”

Without acquiescing to the § 112 rejections, Applicant now asserts that claims 73 and 77 are in condition for allowance. Claims 74-76 and 78-80, which depend upon claim 73, remain in condition for allowance.

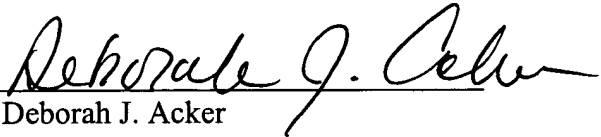
Applicant respectfully requests an early Notice of Allowance of pending claims 73-80. The Examiner is invited to call the undersigned at 650-849-6677, to resolve any minor issues which might remain.

If there are any further fees due in connection with the filing of this Response, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

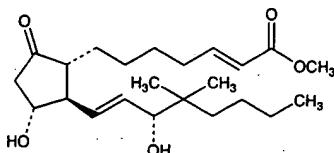
Dated: August 5, 2004

By: 
Deborah J. Acker
Reg. No. 48,916

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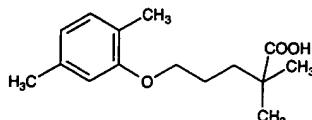
Gemfibrozil

70.02%, H 9.71%, O 20.28%. Analog of prostaglandin E₁, q.v. Prepn: M. Hayashi *et al.*, Ger. pat. 2,700,021 corresp to U.S. pat. 4,052,512 (both 1977 to Ono); H. Suga *et al.*, *Prostaglandins* 15, 907 (1978). Effects on uterine contractility and steroid hormone plasma levels: K. Oshima *et al.*, *J. Reprod. Fertil.* 55, 353 (1979). Effects on reproductive function: K. Matsumoto *et al.*, *Nippon Yakurigaku Zasshi* 79, 15 (1982), C.A. 96, 98392 (1982). Use in termination of first trimester pregnancy: O. Reiertsen *et al.*, *Prostaglandins Leukotrienes Med.* 8, 31 (1982).



Therap Cat: Abortifacient; oxytocic.

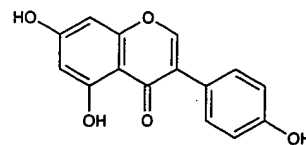
4394. Gemfibrozil. 5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanoic acid; 2,2-dimethyl-5-(2,5-xylyloxy)valeric acid; CI-719; Decrelip; Genlip; Gevilon; Lipozid; Lipur; Lopid. C₁₅H₂₂O₃; mol wt 250.34. C 71.97%, H 8.86%, O 19.17%. Serum lipid regulating agent. Prepn: P. L. Creger, Ger. pat. 1,925,423; *idem*, U.S. pat. 3,674,836 (1969, 1972, both to Parke, Davis). Production: O. P. Goel, U.S. pat. 4,126,637 (1978 to Warner-Lambert). Pharmacology: A. H. Kissebach *et al.*, *Atherosclerosis* 24, 199 (1976); M. T. Kahonen *et al.*, *ibid.* 32, 47 (1979). Series of articles on metabolism, clinical pharmacology, kinetics and toxicology: *Proc. Roy. Soc. Med.* 69, Suppl 2, 1-120 (1976). Toxicity data: S. M. Kurtz *et al.*, *ibid.* 15. Controlled clinical trial in hyperlipidemia: J. E. Lewis *et al.*, *Pract. Cardiol.* 9, 99 (1983). Multicenter clinical trial of long-term effect on coronary heart disease: V. Manninen *et al.*, *J. Am. Med. Assoc.* 260, 641 (1988).



Crystals from hexane, mp 61-63°. bp_{0.02} 158-159°. LD₅₀ in mice, rats (mg/kg): 3162, 4786 orally (Kurtz).

Therap Cat: Antihyperlipoproteinemic.

4395. Genistein. 5,7-Dihydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one; 4',5,7-trihydroxyisoflavone; prunetol; genisteol. C₁₅H₁₀O₅; mol wt 270.24. C 66.67%, H 3.73%, O 29.60%. Phytoestrogen found in soy products; the aglucon of genistin and of sophoricoside, q.v. Specific protein kinase inhibitor. Prepn from the glucoside by hydrolysis with emulsin: Charaux, Rabaté, *J. Pharm. Chim.* [9] 1, 404 (1941); by hydrolysis with HCl in methanol: Walter, *J. Am. Chem. Soc.* 63, 3273 (1941). Isoln from *prunus* spp., *Rosaceae*: Hasegawa *ibid.* 79, 1738 (1957); from *Podocarpus spicata* R.Br., *Podocarpaceae*: Briggs, Cebalo, *Tetrahedron* 6, 145 (1959). Structure: Baker, Robinson, *J. Chem. Soc.* 1925, 1981; 1926, 2713; Walz, *Ann.* 489, 118 (1931). Synthesis: Baker, Robinson, *J. Chem. Soc.* 1928, 3115; Narasimhachari *et al.*, *J. Sci. Ind. Res.* 12, 287 (1953); Yoder *et al.*, *Proc. Iowa Acad. Sci.* 61, 271 (1954); Zemplén *et al.*, *Acta Chim. Acad. Sci. Hung.* 19, 277 (1959). HPLC determn in biological fluids: J. G. Supko, L. R. Phillips, *J. Chromatog. B* 666, 157 (1995); A. A. Franke *et al.*, *Proc. Soc. Exp. Biol. Med.* 208, 18 (1995). Review of synthesis and isotopic labeling: K. Wähälä *et al.*, *ibid.* 27-32. Series of articles on chemopreventive properties and mechanism of action: *ibid.* 103-115, 120-130; *J. Nutr.* 125, Suppl. 3, 777S-797S (1995).



Rectangular or six-sided rods from 60% alcohol. Dendritic needles from ether. mp 297-298° (slight decompn). Sol in the usual organic solvents (Walter, *loc. cit.*); practically insol in water; sol in dil alkalis with yellow color. uv max: 262.5 nm (ε 138). Alkaline hydrolysis yields phloroglucinol and *p*-hydroxyphenylacetic acid.

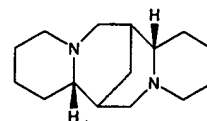
Triacetate, C₁₅H₇O₅(CH₃CO)₃, clusters of needles from alcohol, mp 200-202°. Sol in organic solvents; practically insol in alkalis.

7-D-Glucoside, C₂₁H₂₀O₁₀, *genistin*. For isoln and structure see Walter, Hasegawa, Walz, *loc. cit.* Synthesis: Zemplén, Farkas, *Ber.* 76B, 1110 (1943). Pale yellow plates from 80% ethanol, mp 256°. [α]_D²⁵ -28° (c = 0.6 in 0.02N NaOH); [α]_D²⁵ -21.4° (pyridine). uv max (85% ethanol): 262.5 nm (a 90.5). Practically insol in cold water; slightly sol in hot water, hot ethanol, hot methanol; sol in hot 80% ethanol, hot 80% methanol, hot acetone, pyridine.

4'-Methyl ether, C₁₆H₁₂O₅, 5,7-dihydroxy-4'-methoxyisoflavone; Biochanin A; *olmelin*. Isoln from red clover: Pope *et al.*, *Chem. & Ind. (London)* 1953, 1092; Wong, *J. Sci. Food Agr.* 13, 304 (1962); from *Andira inermis* (Swartz) H.B.K., *Leguminosae*: Crocker *et al.*, *J. Chem. Soc.* 1962, 4906. Identity with *olmelin*: Gakhokidze, *J. Appl. Chem. USSR* 23, 789 (1950), C.A. 46, 9098i (1952). Structure: Bose, Siddiqui, *J. Sci. Ind. Res.* 9B, no. 1, 25 (1950). Synthesis: Baker *et al.*, *Nature* 169, 706 (1952). Yellow needles from methanol, mp 212-216°.

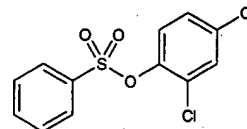
USE: Chemical probe to explore signal transduction pathways.

4396. Genisteine-Alkaloid. [7S-(7α,7aa,14α,14aa)]-Dodecahydro-7,14-methano-2H,6H-dipyridol[1,2-a:1',2'-e]-[1,5]diazocine; 11-isosparteine; *l*-α-isosparteine. C₁₅H₂₆N₂; mol wt 234.38. C 76.87%, H 11.18%, N 11.95%. A stereoisomer of sparteine, q.v., isolated from *Cytisus scoparius* (L.) Link, (*Spartium scoparium* L.), *Leguminosae*: Valeur, *Compt. Rend.* 167, 23, 163 (1918); from *Lupinus caudatus* Kellogg, *Leguminosae*: Marion *et al.*, *Can. J. Chem.* 29, 22 (1951). Identity with *l*-α-isosparteine: Marion, Leonard, *ibid.* 297. Structure: Leonard *et al.*, *J. Am. Chem. Soc.* 77, 1552 (1955). Absolute configuration: Okuda, Tsuda, *Chem. & Ind. (London)* 1961, 1115.



Monohydrate, needles from boiling acetone, mp 108-110°. [α]_D²⁵ -51.6° (c = 0.7 in abs ethanol).

4397. Genite®. 2,4-Dichlorophenol benzenesulfonate; benzenesulfonic acid 2,4-dichlorophenyl ester; 2,4-dichlorophenyl benzenesulfonate; EM-923; Genitol 923. C₁₂H₇Cl₂O₃S; mol wt 303.17. C 47.54%, H 2.66%, Cl 23.39%, O 15.83%, S 10.58%. Prepn: Gilbert, U.S. pat. 2,618,583 (1952 to Allied Chemical).



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